Drugs affecting the nervous system

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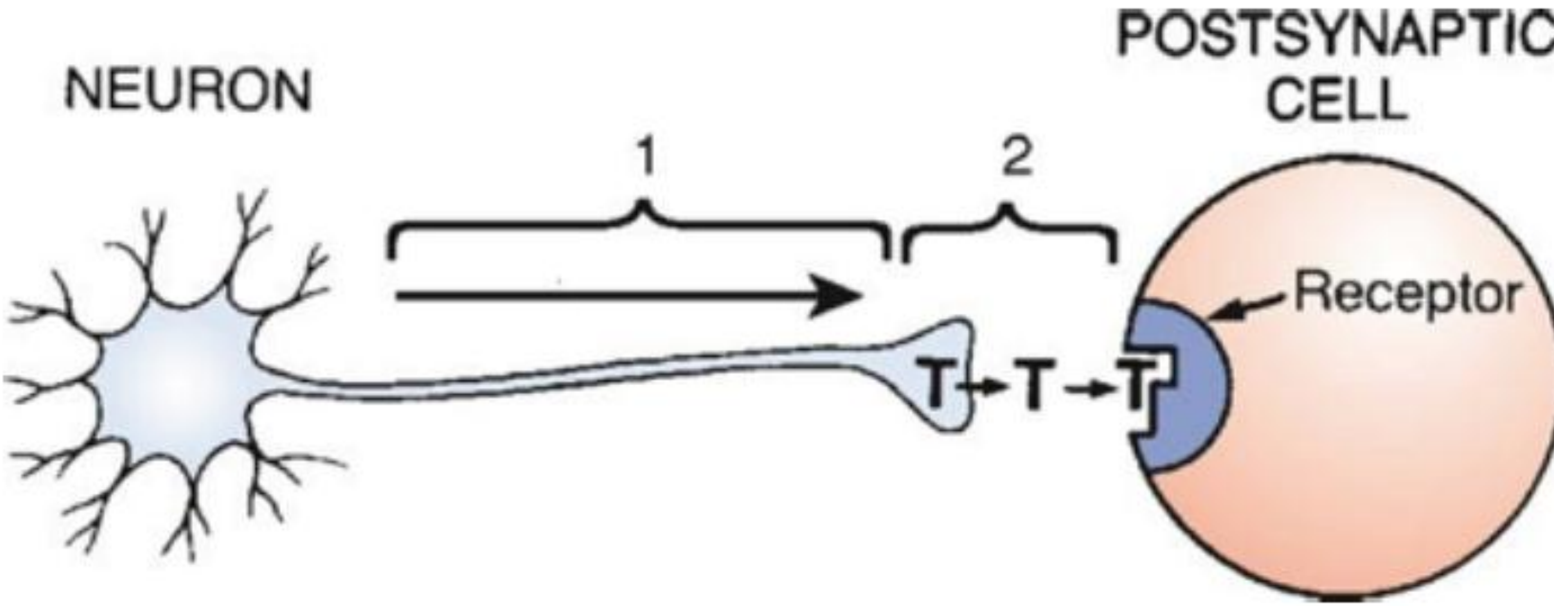
Learning objectives

For common drugs acting on the nervous system, the student will be able to:

- Discuss the mechanism of action of the drug
- Point out indication/s of the drug
- Identify possible adverse reactions of the drug
- Relate contraindications to the drug
- Discuss potential interactions and toxic effects of the drug
- Explain common considerations and corresponding nursing responsibilities for specific types of drugs

Review of nervous system

Figure 12-1 **How neurons regulate other cells.** There are two basic steps in the process by which neurons elicit responses from other cells: (1) axonal conduction and (2) synaptic transmission. (T = neurotransmitter.)



Basic mechanisms by which neuropharmacologic agents act

- Sites of action
  - Axonal conduction
  - Synaptic transmission

Axonal conduction

- Drugs that act by altering axonal conduction are not very selective.
- Local anesthetics are the only drugs proved to work by altering (decreasing) axonal conduction.
- Because these agents produce nonselective inhibition of axonal conduction, they suppress transmission in any nerve they reach

Synaptic transmission

- Drugs that alter synaptic transmission can produce effects that are highly selective.
- Synapses, unlike axons, differ from one another.
- Synapses at different sites employ different transmitters.
- In addition, for most transmitters, the body employs more than one type of receptor.

Receptor

- The ability of a neuron to influence the behavior of another cell depends, ultimately, upon the ability of that neuron to alter receptor activity on the target cell.

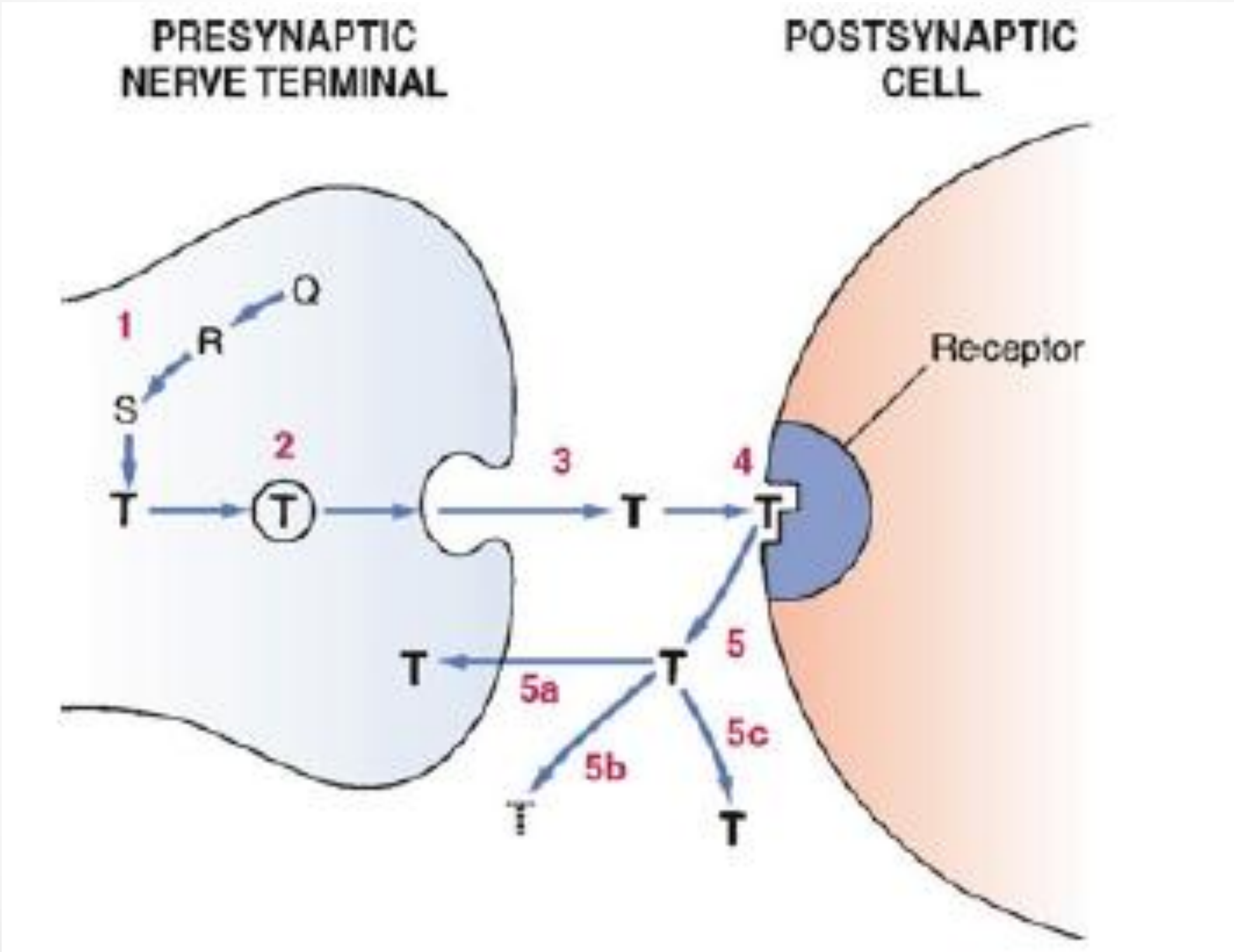
Therefore:

The impact of a drug on a neuronally regulated process is dependent on the ability of that drug to directly or indirectly influence receptor activity on target cells.

Steps in synaptic transmission

Step 1.	Transmitter synthesis
Step 2.	Transmitter storage
Step 3.	Transmitter release
Step 4.	Receptor binding
Step 5.	Termination of transmission

Steps in synaptic transmission



Step 1. Synthesis of transmitter (T) from precursor molecules (Q, R, and S).

Step 2. Storage of transmitter in vesicles.

Step 3. Release of transmitter: In response to an action potential, vesicles fuse with the terminal membrane and discharge their contents into the synaptic gap.

Step 4. Action at receptor: Transmitter binds (reversibly) to its receptor on the postsynaptic cell, causing a response in that cell.

Step 5. Termination of transmission: Transmitter dissociates from its receptor and is then removed from the synaptic gap by

(a) reuptake into the nerve terminal,
(b) enzymatic degradation, or
(c) diffusion away from the gap.

Effects of drugs on the steps in synaptic transmission

- Because synaptic transmission has multiple steps, the process offers a number of potential targets for drugs.

- Drugs may act as an agonist or antagonist at receptor site

- Note that activation of a receptor does not necessarily mean that a physiologic process will go faster; receptor activation can also make a process go slower.

TABLE 12-1 Effects of Drugs on Synaptic Transmission and the Resulting Impact on Receptor Activation

Step of Synaptic Transmission	Drug Action	Impact on Receptor Activation*
1. Synthesis of transmitter	Increased synthesis of T	Increase
	Decreased synthesis of T	Decrease
	Synthesis of "super" T	Increase
2. Storage of transmitter	Reduced storage of T	Decrease
3. Release of transmitter	Promotion of T release	Increase
	Inhibition of T release	Decrease
4. Binding to receptor	Direct receptor activation	Increase
	Enhanced response to T	Increase
	Blockade of T binding	Decrease
5. Termination of transmission	Blockade of T reuptake	Increase
	Inhibition of T breakdown	Increase

T = transmitter.

* Receptor activation is defined as producing an effect equivalent to that produced by the natural transmitter that acts on a particular receptor.

- Transmitter synthesis
  - ➢ Increase in synthesis of T – increase in T in vesicles – when action potential reaches axon terminal, more T released, more T available to activate receptors
  - ➢ Decrease in synthesis of T – decrease T in vesicles – less T released – less T available to activate receptors
  - ➢ Some drugs can cause neurons to synthesize T whose structure is different from that of normal T molecules - “super” transmitters - release of super T increase receptor activation

- Transmitter storage
- Transmitter release
- Receptor binding
  (1) bind to receptors and cause activation
  (2) bind to receptors and thereby block receptor activation by other agents

- Receptor binding

  (3) bind to receptor components and thereby enhance receptor activation by the natural transmitter at the site

Direct acting receptor drugs

Agonists

- morphine (used for its effects on the CNS)
- epinephrine (used mainly for its effects on the cardiovascular system)
- insulin (used for its effects in diabetes)

Antagonists

- naloxone (used to treat overdose with morphine-like drugs)
- antihistamines (used to treat allergic disorders)
- propranolol (used to treat hypertension, angina pectoris, and cardiac dysrhythmias)

Direct acting receptor drugs

Drugs which bind to receptor components and enhance the actions of natural transmitter

- Benzodiazepines (e.g. diazepam) - drugs in this family and related agents are used to treat anxiety, seizure disorders and muscle spasms

Termination of transmission

(1)Blockade of transmitter reuptake
(2)Inhibition of transmitter degradation

Drugs that act by either mechanism will cause the concentration of transmitter in the synaptic gap to rise, thereby causing receptor activation to increase.

Peripheral nervous system function

Two basic types of information

First, you need to know the types of receptors through which the peripheral nervous system works when influencing the function of a specific organ.

Second, you need to know what the normal response to activation of those receptors is.

Three types of information for PNS drugs

(1) the type (or types) of receptor through which the drug acts;

(2) the normal response to activation of those receptors; and

(3) what the drug in question does to receptor function (i.e. increase or decrease receptor activation).

Autonomic nervous system functions

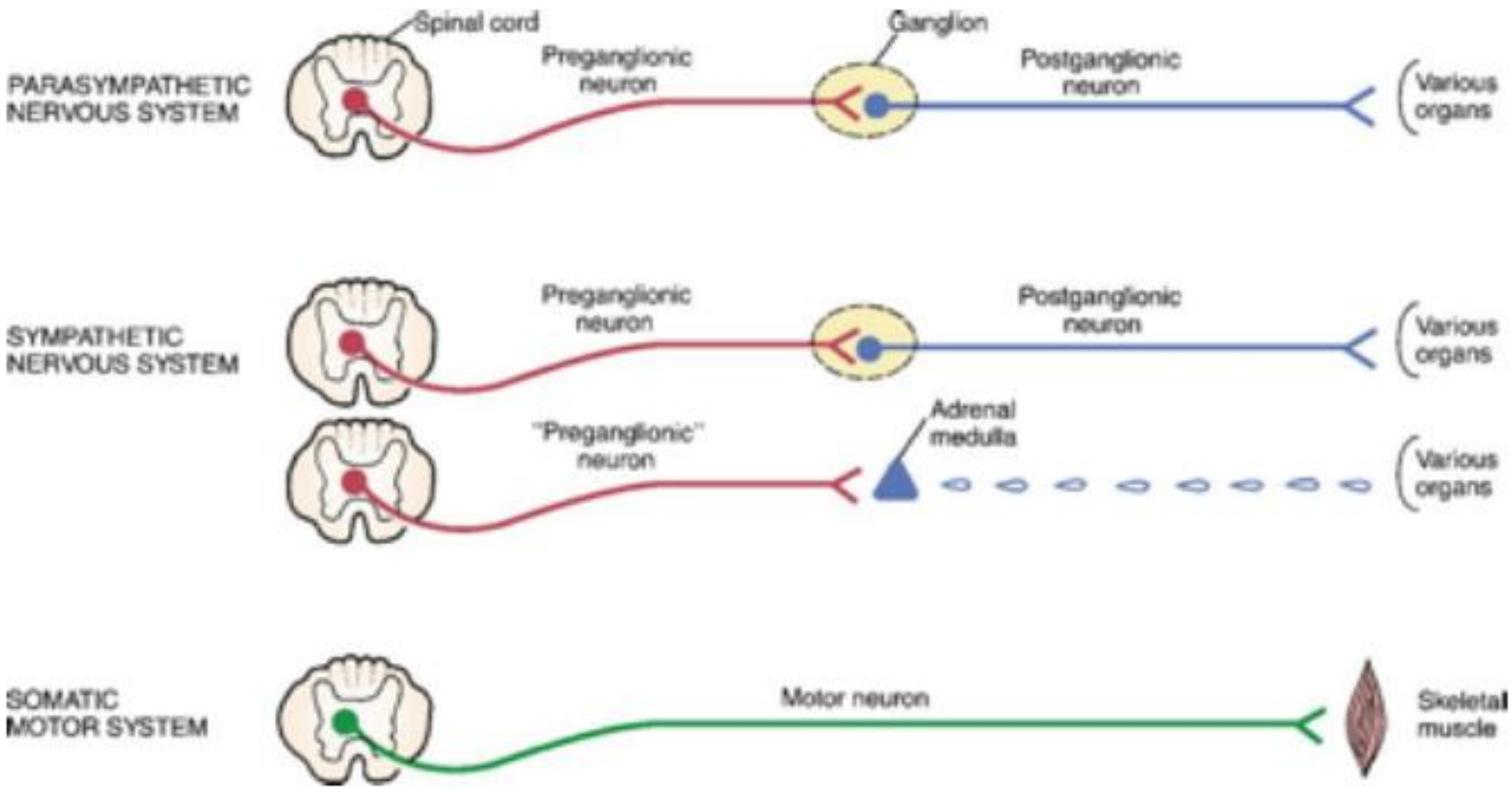
- regulation of the heart;
- regulation of secretory glands (salivary, gastric, sweat, and bronchial glands); and
- regulation of smooth muscles (muscles of the bronchi, blood vessels, urogenital system and GI tract).

Table 7.3 Effects of the Sympathetic and Parasympathetic Divisions of the Autonomic Nervous System

Target organ/system	Parasympathetic effects	Sympathetic effects
Digestive system	Increases smooth muscle mobility (peristalsis) and amount of secretion by digestive system glands; relaxes sphincters	Decreases activity of digestive system and constricts digestive system sphincters (for example, anal sphincter)
Liver	No effect	Causes glucose to be released to blood
Lungs	Constricts bronchioles	Dilates bronchioles
Urinary bladder/urethra	Relaxes sphincters (allows voiding)	Constricts sphincters (prevents voiding)
Kidneys	No effect	Decreases urine output
Heart	Decreases rate; slows and steadies	Increases rate and force of heartbeat
Blood vessels	No effect on most blood vessels	Constricts blood vessels in viscera and skin (dilates those in skeletal muscle and heart); increases blood pressure
Glands—salivary, lacrimal, gastric	Stimulates; increases production of saliva, tears, and gastric juice	Inhibits; result is dry mouth and dry eyes

Target organ/ system	Parasympathetic effects	Sympathetic effects
Eye (iris)	Stimulates constrictor muscles; constricts pupils	Stimulates dilator muscles; dilates pupils
Eye (ciliary muscle)	Stimulates to increase bulging of lens for close vision	Inhibits; decreases bulging of lens; prepares for distant vision
Adrenal medulla	No effect	Stimulates medulla cells to secrete epinephrine and norepinephrine
Sweat glands of skin	No effect	Stimulates to produce perspiration
Arrector pili muscles attached to hair follicles	No effect	Stimulates; produces "goose bumps"
Penis	Causes erection due to vasodilation	Causes ejaculation (emission of semen)
Cellular metabolism	No effect	Increases metabolic rate; increases blood sugar levels; stimulates fat breakdown
Adipose tissue	No effect	Stimulates fat breakdown

Figure 13-3 The basic anatomy of the parasympathetic and sympathetic nervous systems and the somatic motor system.



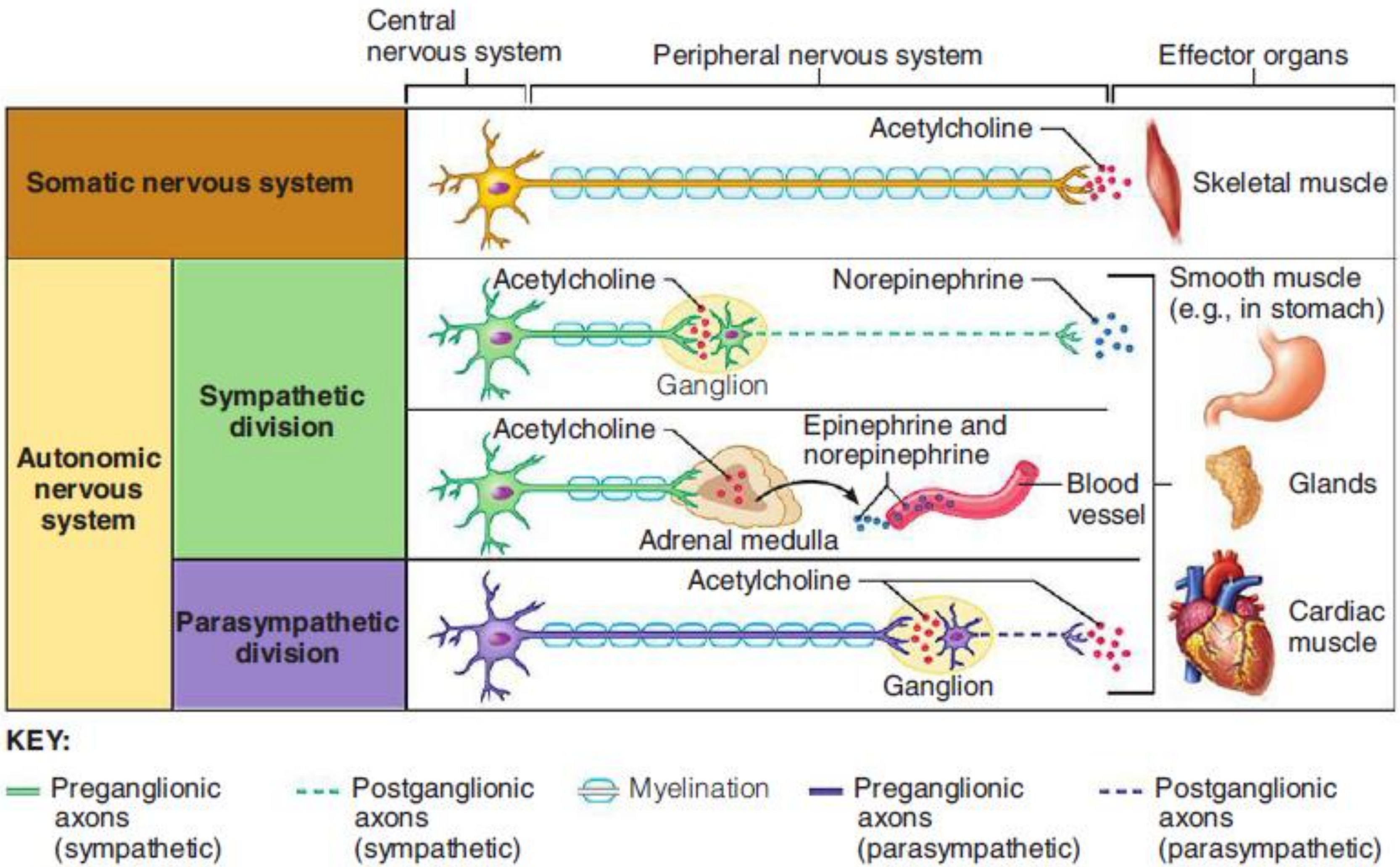


Figure 7.27 **Comparison of the somatic and autonomic nervous systems.**

PNS Transmitters

- Three neurotransmitters: *acetycholine (ACh), norepinephrine, epinephrine*
- *Acetycholine* released by
  1. all preganglionic neurons of parasympathetic and sympathetic nervous system
  2. all postganglionic neurons of parasympathetic nervous system
  3. all motor neurons to skeletal muscles
  4. most postganglionic neurons of sympathetic nervous system that go to sweat glands

PNS Transmitters

- *Norepinephrine* released by all postganglionic neurons of sympathetic nervous system except those which go to sweat glands (ACh)

- *Epinephrine* is major transmitter released by adrenal medulla. Adrenal medulla also releases some norepinephrine.

PNS Receptors

- Cholinergic receptors – mediate responses at all junctions where acetycholine is the neurotransmitter
- Adrenergic receptors – mediate responses at all junctions where epinephrine (adrenaline) or norepinephrine is the neurotransmitter

Figure 13-4 **Transmitters employed at specific junctions of the peripheral nervous system.** Summary:

1. *All preganglionic* neurons of the *parasympathetic* and *sympathetic* nervous systems release *acetylcholine* as their transmitter.

2. *All postganglionic* neurons of the *parasympathetic* nervous system release *acetylcholine* as their transmitter.

3. *Most postganglionic* neurons of the *sympathetic* nervous system release norepinephrine as their transmitter.

4. *Postganglionic* neurons of the sympathetic nervous system that innervate *sweat glands* release *acetylcholine* as their transmitter.

5. *Epinephrine* is the principal transmitter released by the *adrenal medulla*.

6. *All motor neurons* to *skeletal muscles* release *acetylcholine* as their transmitter.

Receptor subtypes

- Three major subtypes of cholinergic receptors
  - Nicotinic$_N$
  - Nicotinic$_M$
  - Muscarinic
- Four major subtypes of adrenergic receptors
  - Alpha$_1$
  - Alpha$_2$
  - Beta$_1$
  - Beta$_2$

How do we know receptor subtypes exist?

- Experiment with acetylcholine and a series of drugs (including nicotine and atropine) on two tissues: skeletal and ciliary muscle
- What do the effects of nicotine on skeletal muscle and ciliary muscle suggest?

  (1) Because skeletal muscle contracts when nicotine is applied, we can conclude that skeletal muscle has receptors at which nicotine can act.

  (2) Because ciliary muscle does not respond to nicotine, we can tentatively conclude that ciliary muscle does not have receptors for nicotine.

How do we know receptor subtypes exist?

- What do the effects of nicotine on skeletal muscle and ciliary muscle suggest?
  - (3) Both types of muscle have receptors for acetylcholine and because nicotine appears to act only at the acetylcholine receptors on skeletal muscle, we can tentatively conclude that the acetylcholine receptors on skeletal muscle are different from the acetylcholine receptors on ciliary muscle.

How do we know receptor subtypes exist?

- What do the effects of atropine on skeletal muscle and ciliary muscle suggest?

  Pretreatment with atropine selectively blocks the response to acetylcholine in ciliary muscle—but atropine does nothing to prevent acetylcholine from stimulating receptors on skeletal muscle

  Atropine can selectively block cholinergic receptors in ciliary muscle, we can conclude with certainty that the receptors for acetylcholine in these two types of muscle must be different.

Figure 13-6 **Locations of cholinergic and adrenergic receptor subtypes.** Summary:

1. *Nicotinic*$_N$ receptors are located on the *cell bodies of all postganglionic neurons* of the *parasympathetic* and *sympathetic* nervous systems. *Nicotinic*$_N$ receptors are also located on cells of the adrenal *medulla*.

2. *Nicotinic*$_M$ receptors are located on *skeletal muscle*.

3. *Muscarinic* receptors are located on *all organs* regulated by the *parasympathetic* nervous system (ie, organs innervated by postganglionic parasympathetic nerves). *Muscarinic* receptors are also located on *sweat glands*.

4. *Adrenergic* receptors—*alpha, beta,* or both—are located on *all organs* (except sweat glands) regulated by the *sympathetic* nervous system (ie, organs innervated by postganglionic sympathetic nerves). *Adrenergic* receptors are also located on organs regulated by epinephrine released from the *adrenal medulla*.